lip recently reported by Shamberg in Philadelphia, in which one young fellow was the source of infection of six girls and one boy, at a kissing party, the use of salvarsan is indicated.[1] The rapid healing effect which salvarsan has upon any syphilitic affection of the mucous membranes will, in just such instances, quickly lessen the danger of spreading the infection.

Too much praise cannot be given Ehrlich's discovery for its effect upon stubborn, resistent, luetic lesions. A palmar syphilid that has for months resisted rubs, injections, mercury and potassium iodid by mouth combined with hygienic and systemic treatment, can be changed for the better within twenty-four hours with one dose of salvarsan intravenously administered. The whole palm or sole may be smooth in a few days, and the patient will think the physician a wonder. It is the drug that is the wonder. Like all other things that come in groups, recently three such cases with involvement of the palm or sole or both, presented themselves, and all healed marvelously quickly after a single injection of salvarsan in each.

Affections of the mucous membranes may be as stubborn as those of the palm or sole, as in one instance within the last few months in which the man gave a history of an infection four years ago. He had had almost continuous treatment, with only short intervals, during the last two years, and interesting to relate, at the end of each interval almost the whole mouth would break out in a monster herpetic eruption, which was almost deadly in its interference with eating, and was with difficulty controlled by mercury. One dose of salvarsan cleared this up almost completely in four days. Improvement occurred in less than twenty-four hours. He has been free since the treatment.

Syphilitic papillomata and cutaneous gummata yield wonderfully kindly to salvarsan, and it is a boon to the patient with malignant syphilis. Many a perforation of the hard palate can be prevented by the use of this remedy.

Contrary to the experience of some who are using salvarsan quite extensively, I have not found it necessary to repeat the dose very many times in any one patient, but it has been necessary to give mercury after the salvarsan. We do not yet know that a cure is possible with one, two, three, or even seven doses, and I think it a serious error to consider it an absolute specific.

A most interesting and instructive lesson will, no doubt, be learned by all of us, that there are some cases which will not yield readily to mercury and kali iodid, and will not yield to the additional use of salvarsan, but will in the end react most pleasingly to mercurial treatment or mixed treatment after the use of this drug. I saw this result from the use of atoxyl before we knew salvarsan, in a patient with chancre of the lip and such severe joint pains that he was confined to bed several weeks. Mercury alone did not relieve him and kali iodid had no effect. After three injections of three grains each of atoxyl he improved rapidly under mercury. Nearly two years later this same man had resistent lesions of the mucous membranes which yielded readily to salvarsan. It would seem that the wonderful tonic effect of the arsenic renders the patient more amenable to the effects of mercury and kali iodid. I firmly believe we are doing a great injustice in not following or attempting to follow this method of procedure before repeating the administration of so intense a remedy, and then should it fail, a second or even a third dose of salvarsan is not only indicated, but is almost obligatory.

I should like to express a thought that has been impressed upon me that we owe it to the patient not to become so enthusiastic about salvarsan, and not to depend so wholly upon it that he will lose his confidence in this remedy. I mean this: the layman has already learned that salvarsan does not always cure, and that it has to be repeated, and he knows that it sometimes fails completely, and just in proportion to what wonderful things he was led at first to expect he will lose faith in the new drug and consider it far less important than it deserves. I speak of this because only recently two patients with conditions that have stubbornly resisted the old line of treatment have objected to the use of salvarsan for these reasons, and one dose in each case would in all probability bring about complete healing. Might we not prevent this loss of confidence in the remedy by the systematic use of the combined specifics?

As a last word, I believe that salvarsan is one of the greatest drugs we have in medicine, and it increases rather than lessens my respect for mercury and iodid of potash. I recall a story told by my colleague, Dr. Douglass W. Montgomery, in reference to kali iodid. Ricord, with some friends, had a box at a theatre in Paris, when one of the noted prima donnas sang. He applauded heartily with the rest, but continued his applause even after the others had stopped. His friends wondered at this and asked him the reason for his enthusiasm. He answered, "My appreciation is not wholly for the fair lady, I am applauding iodid of potash."

[1] An Epidemic of Chancres of the Lip from Kissing, by Jay F. Schamberg, Jour. of A. M. A., Sept. 2, 1911.

AN EXPERIMENTAL STUDY OF A REMARKABLE CASE OF NEPHRITIS WITH EMPYEMA OF THE CRANIAL SINUSES AND MILKY SERUM.

(Contribution to the Literature of Fat Metabolism.)

By CLARENCE QUINAN, M. D., San Francisco.

In the course of a series of experiments upon the blood and urine proteins of a nephritic man, a peculiar lipemia was brought to light. The main facts observed during a biochemical inquiry into this condition are here brought together.

History: M. V., aet. 32, a Russian, by occupation a cook. The family history is negative. His father, mother, six brothers and one sister are living and well. Until about the twentieth year his personal history was uneventful. Prior to that age he enjoyed vigorous health. He has never had any

venereal infection. Some time in his twentieth year there was a purulent discharge from the left ear which entirely diappeared after a radical mastoid operation. Twelve years after this operation, in 1910, he first noticed swelling of the ankles. Rest in bed was ordered, together with a diet of milk, eggs and bread. At the end of three weeks the dropsy showed little improvement and he was advised to enter a hospital. The succeeding four months were spent in three different hospitals. In the first, he received diuretic treatment, and his food consisted of fried ham, or bacon, with eggs and milk three times a day. Elsewhere, he had sweat baths, and milk diets, variously modified, but he lost weight steadily and returned to his home very weak. The dropsy persisted.

He asserts that for a number of years he has been subject to nose-bleed, periodically, especially in warm weather. Since the edema made its appearance, however, the nasal hemorrhages have been more frequent. He has had at times several in the course of a week and, exceptionally, as many as four or five in one day. Occasionally, the bleeding has awakened him at night by giving rise to a tickling sensation in the throat. (It should be stated here that the history of persistent epistaxis was elicited at a time when the experimental work upon this man was far advanced. There never was any evidence of it at the bedside, and as the man had no nurse, and made no complaint of it, the symptom long was unsuspected. The actual loss of blood from this source probably was insignificant, or the condition certainly must have awakened suspicion during his stay in various hospital wards.)

The patient was first seen March 20th, 1911. At that time he was confined to his bed and presented the characteristic picture of chronic parenchymatous nephritis.

Physical examination: He is a man of medium height, broad-shouldered and well-formed, but considerably emaciated. The spinous processes of the vertebrae are very much in evidence and his ribs show plainly. Contrariwise, the face looks quite full, and the lower extremities are swollen and edematous. The skin everywhere has an unhealthy, muddy appearance, which is greatly accentuated by personal uncleanliness and the presence of acne vulgaris. The skin is puffy under the eyes.

All his special senses are normal, and there are no central or peripheral symptoms referable to the cranial nerves. The eye grounds are entirely negative. Behind the left ear is an old trephine opening at the site of the mastoid antrum. There is no discharge from it or the middle ear. The mouth and throat are negative: he has good teeth, the palate is well arched, and the tonsils are not enlarged.

The lungs are normal. The heart is normal in size and position. There is no arrythmia, and the apex impulse is not exaggerated. All the valve sounds are clear. The second aortic sound is perhaps slightly accentuated. The radial pulse rate is eighty, and the vessel wall is soft and easily compressible. The liver and spleen are not enlarged.

There is massive edema of the lower extremities. Sensation everywhere is intact, and the reflexes are normal. The temperature is normal. The blood contains 80% of hemoglobin.

Urine: Specific gravity, 1.014; albumen, 6 parts per mille; no sugar. The sediment contains numerour coarsely granular casts, epithelia cells, etc., and is characteristic of chronic parenchymatous nephritis. The daily volume was about 2500 cubic centimeters.

CHARACTERISTICS OF THE MILKY SERUM

The fresh blood of this individual was not in any way remarkable. It appeared, in fact, to be entirely normal. On standing, however, in a very short time white, milky serum began to separate, and, generally speaking, in the course of an hour it had accumulated in such abundance that nothing whatever could be seen of the clot, and the vessel appeared to contain pure milk. The fresh serum was slightly alkaline in reaction. It showed no tendency to separate into layers on standing, and after several weeks in vitro remained homeogeneous in appearance and uniformly white. It was not affected in the least by ordinary filtration. And it passed without change through a Berkfeld filter. When diluted in the proportion of one to one hundred with distilled water, it formed a strongly opalescent solution. This mixture was remarkably stable. Weak mineral acids and alkalies had no demonstrable effect upon it and various neutral salts brought about no change that could be detected. All attempts to clarify it by means of organic fat solvents, failed utterly. When, on the contrary, the serum, diluted with fifteen parts of water was gently mixed with chloroform, so far from rendering the solution clear this solvent invariably had the reverse effect and augmented the cloudiness. By treating the milky serum as Boggs and Norris suggested, (Jour. Exp. Med., 11, 553, 1909), with an excess of ammonium oxalate crystals, and allowing it to stand 12 hours, ether, previously tried without success, rendered the serum quite clear, but it was invariably noted, also, that after a few hours the serum emitted an intense ammoniacal odor, exactly as would have occurred in an ordinary double decomposition in the presence of a stronger inorganic base.

The diluted serum could always be clarified by filtering out the carbon dioxide globulin group.

METHODS AND TECHNIC.

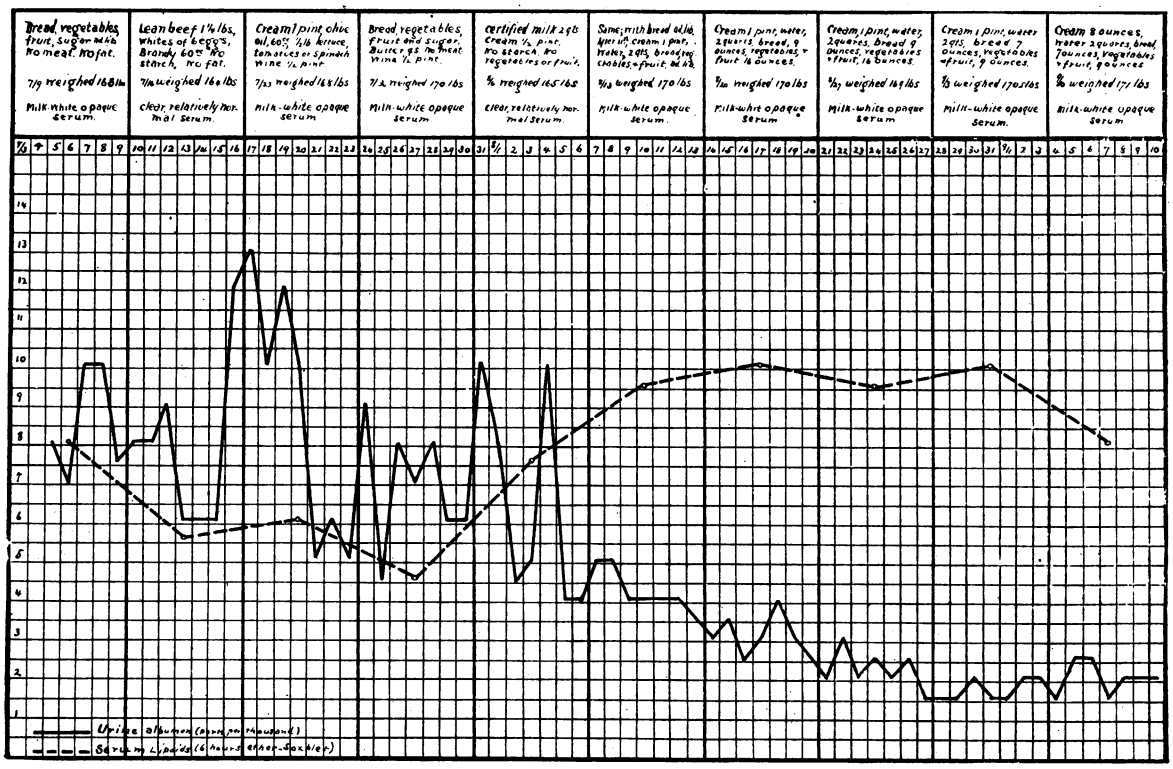
From ten to forty cubic centimeters of blood were taken, as needed, in the usual manner, once or twice a week. The serum was measured with a capillary pipette divided into tenths.

In all direct extractions, one cubic centimeter of serum was used. It is perhaps as well to state that by a direct extraction is meant one in which the serum is dropped into an excess of the solvent Naturally, ether and chloroform cannot be employed for this purpose.

In regular Soxhlet extractions with ether alone, and in serial extractions with the four principal lipoid solvents, ether, chloroform, acetone and absolute alcohol, two cubic centimeters of serum were used.

On the continent, according to the most recent reports, it is the custom to dry the serum on strips of filter paper before proceeding to extract it in the usual way. It is, however, a very debatable question whether, as Friedemann and Herzfeld appear to believe, (Berl. klin. Woch., No. 47, 1911), the dry film of protein can be penetrated by the solvents and completely extracted in so short a time as half an hour. A more satisfactory plan than this is to incorporate the fresh serum with calcined kieselguhr, which holds the watery part of the serum firmly but does not oppose any resistance to the free passage of the solvent whilst, besides, it affords a very large contact surface to the reagent.

The figures upon which the lipoid curve in table 1 is based were obtained by ether extraction of the dry kieselguhr-serum mixture, continued for six hours. In a series of studies at present under way, however, the ether method has given place to one which yields the total lipoid value. A description of this method for the determination of the total lipoids appeared in an earlier issue of this Journal.



A point to be emphasized is that by ether alone it is not possible to remove all lipoids. Indeed, no one solvent will accomplish this.

The cholesterin ester was saponified with alcoholic soda at 100° Centigrade. The free cholesterin was taken up with chloroform which was then dehydrated with strong sulphuric acid. For a successful result, of course, the dehydration must be thorough.

EXPERIMENTAL OBSERVATIONS CONCERNING THE RELATION OF THE LIPEMIA TO THE FOOD-FAT, ETC.

The various test diets given during a period of ten weeks, and the corresponding peculiarities of the urine-albumen and serum-lipoid curves, are graphically shown in Table 1.

Speaking in a general way of the entire period, it may be said that in proportion as protein substances were excluded from the diet, the albuminuria steadily decreased. But, curiously enough, to insure the physical comfort of the patient, and to keep his weight constant, it was found to be necessary at the same time to maintain a high grade of lipemia. This end was finally attained by a carefully adjusted regimen of cream and carbohydrates.

It will be noted that the highest lipoid value recorded in the curve was a little over 2%. This, however, since it is the ether value alone, does not represent the total lipoid value at that point. The true value there was nearly 3.20%.

Another interesting fact observed was that a progressive reduction of the specific gravity took place without a corresponding increase of the urine volume. In ten weeks the density decreased from 1.014 to 1.006, but the volume ranged only between 2000 and 2500 cubic centimeters.

The urine was tested for sugar daily with dilute Fehling's solution, and with Nylander's reagent. And once a week a fermentation test was made with controls. A positive fermentation test was twice noted, once in the first, and again towards the end of the second week. At other times the tests were negative. The amount of sugar present was, however, very small, and would ordinarily be reported as a trace.

One of the most significant facts brought out in the course of this work, and the one upon which it is desired to lay especial emphasis, was that the lipemia could be abolished by diet control.

This singular fact was first observed whilst the patient was limited to a strictly protein diet. During that week the serum was almost clear and only a trace of cloudiness remained. At the same time, however, the man lost weight rapidly, the skin assumed a muddy appearance, and he was moody and despondent. Moreover, at the end of this week, as it was natural to expect, there was an enormous increase in the albuminuria. The disturbance caused by this diet lasted over to the middle of the following, third week, when his subjective condition greatly improved and the albumen output diminished notably.

The serum again became clear in the fifth week. This time, strange to say, when the diet consisted only of milk and cream. During this week he consumed each day two quarts of certified milk and one pint of cream. In addition to this, no other food whatever was taken. On this diet, within two days the serum ceased to be milky, and appeared in every respect as it had during the all-protein period. Moreover, again, as in that period, he lost weight rapidly, and the same subjective and objective status re-appeared. At the close of

the milk and cream week, the evidence then pointing clearly to the fact that in order to utilize fat it was necessary for starch to be present, the diet was modified by the addition of a liberal allowance of bread. In a few hours after this starchy food was ingested the serum again became perfectly white. At the same time the change in his general condition was striking. Color returned to his skin and he became cheerful. The weight lost during the milk and cream week was promptly regained when he resumed a diet in which fat and starch predominated. From these experiences it was obvious that in this individual a massive cleavage of fat could not occur in the absence of a starch element, but, unfortunately, the phenomenon had not been studied by weight.

After the ten weeks period was over, therefore, in order to be sure that the foregoing observation was valid, the experiment was repeated, this time with definite lipoid determinations. Exactly the same phenomenon was noted. The details of the experiment are as follows:

Sept. 21st, at noon, before eating, and five hours after the morning meal, the blood was taken. The total lipoid value of this serum was 3.25%. The serum was as white as milk. Sept. 23rd, blood was taken at the same hour. The conditions were the same as before. In the interval, the daily diet had consisted of two quarts of milk, and one pint of cream. The total lipoid value of this specimen was 1.35%. The serum was practically clear and showed only a slight cloudiness. This was at noon. With the mid-day portion of milk and cream which he was then ready to eat, he was allowed all the bread he desired. At two o'clock, 2 hours after eating, the second specimen of blood was taken. Even in this short time, however, the lipoid value had risen to 2.20%. The serum was perfectly white and offered a most extraordinary contrast to the earlier specimen.

The subsequent history of this patient was interesting. Although his general condition was much improved by the dietary restriction, and he had gained in weight, the attacks of nose-bleed continued to annoy him. In order if possible to discover the causative lesion, therefore, a thorough exploration of the nasal cavity was made by Dr. Henry Horn. What was at first supposed to be an idiopathic ulcer of the septum was encountered. It was evidently of long-standing. The tissues about it bled freely when disturbed, and the hemorrhage was rather difficult to control. Somewhat later an accumulation of foul pus was discovered in the antrum of Highmore on the right side and the cavity was drained by a radical operation. As a result of this treatment, the epistaxis ceased directly, and within ten days the blood-serum became practically clear. At the present time, two months after the operation, the serum remains clear, and when blood is taken after a full meal it is not at all milky. The total lipoid value now is slightly less than 1.40%, an enormous reduction when it is considered that at one time the serum contained nearly four per cent. of fatty bodies.

The patient now weighs one hundred and eighty pounds, and continues to take a diet which largely consists of cream, green vegetables and fruit. The albuminuria persists.

The etiology of the peculiar lipemia here described is obscure. About the only conclusion so far tenable, and that a very general one, is, that the experimental data indicate a profound disturbance of a lipolytic mechanism. Perhaps the most conspicuous feature emphasized in the descriptive curves is the protectory action of the lipoids upon the protein substances of the body. Upon this point the evidence was clear and unmistakable. Whenever by dietary restrictions the lipemia was suppressed, the albuminuria was greatly augmented and an immediate loss of weight took place. Conversely, with an increasing lipemia the loss of albumen was noticeably reduced.

By excessive and repeated blood-letting, Boggs and Norris (loc. cit.) were able to produce a very remarkable lipemia in rabbits. There can be no doubt that the white serum so obtained, in many ways was analogous to the serum of this patient. However, the profound secondary anemia induced in the animal as a provocative lesion, did not enter as a noteworthy factor in the human subject, and there was in the latter, moreover, an obvious relation between the lipemic status and the sinus empyema. But here again the evidence leads one astray, for in other patients with sinus empyema, investigated by Dr. Horn, no visible lipemia was detected, and the blood appeared to be normal. A man with a very high grade of lipemia, now being studied, has parenchymatous nephritis, but he is not anemic, nor is there any evidence of sinus disease. Hence it would appear that a disturbance of the lipolytic system, such as that here dealt with, is highly individual and depends upon a pathological substratum at present unknown.

The general conclusion towards which the experimental data here stated appear to trend is that an intravascular lipoid current exists and that it is recruited from the food-fats through the agency of a carbohydrate derivative. In view of the fact that cholesterin esters were present in excess, the lipemia, after the Chauffard school, could be defined as expressive of a true hypercholesterinemia.

IMPORTANT NOTICE!

If you are threatened with a suit for alleged malpractice, communicate at once with the Secretary; many threatened suits are thus averted.

If you are sued notify the Secretary immediately.

DR. PHILIP MILLS JONES,
Secretary,
Butler Building, San Francisco, Cal.